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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 07/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,540	HOGG ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9-12,14-34,38 and 44-68* is/are pending in the application.

4a) Of the above claim(s) *15-17,26-34,44,45,48-53 and 62-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11,12,14 and 38* is/are rejected.

7)☒ Claim(s) *9,10,18-25,46,47 and 54-61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/19/02,12/16/02,6/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 9-12, 14-34, 38, and 44-68 are pending, with claims 2-8, 13, 35-37, and 39-43 cancelled by amendment.

Election/Restrictions

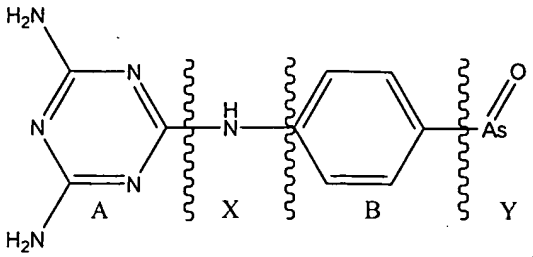
Applicant's election without traverse of Group I, and election of the species GSAO (formula V), as found in claim 21, in the reply filed on May 9, 2005 is acknowledged.

Applicant states that the compound is readable upon claims 1, 9-12, 14-21, 23, 24, 30-34, 38 and new claims 44-57, 59-60 and 62-68. Claims 1, 9-12, 14-21, 23, 24, 30-34, 38, 44-57, 59-60 and 62-68 have been examined on the merits insofar as they read on the elected species.

The examiner notes that while claims 1 and 45 differ only by the generic definitions of A (claim 1 recites amine as an element, which is absent from claim 45) dependent claims 46, 47, and 54-61 are duplicates of claims 9, 10, and 18-25, respectively, and is addressed below (see *Claim Objections*).

The examiner has determined that the elected species, GSAO (formula V), is allowable over the prior art (see *Allowable Subject Matter*, below). The Examiner extended the search to embrace the compounds of claims 18-20 and 22-25 (formulae III, VI, and VII), and has determined that the compounds embraced by claims 18-20 and 22-25 are allowable over the prior art (see *Allowable Subject Matter*, below).

The Examiner has extended the search to the following compound:



, where A comprises hydrophilic amines, and is not a hydrophilic amine *per se*. The proviso of claim 1 requires that when Y is arsenoxide A is not a hydrophilic amine, but does not disallow the structure where A comprises hydrophilic amines. The compound is readable upon **claims 1, 11, 12, 14, and 38**. **Claims 9, 10, 18-25, 46, 47, and 54-61** stand objected to (see *Claim Objections*, below).

Claims 15-17,26-34,44,45,48-53 and 62-68 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 9, 2005.

Claims 1, 11, 12, 14, and 38 have been examined on the merits.

Claim Objections

Claims 46, 47, and 54-61 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 9, 10, and 18-25, respectively.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In the instant case, although independent claims 1 and 45 differ in their definitions of 'A', the subgenus and species of the independent claims are of an overlapping scope, wherein one could not distinguish one claimed structure, or subgenus, from another.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 11, 12, 14, and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, no that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus (MPEP § 2163). If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus (MPEP § 2163). Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*.

In the instant case, the claims are drawn to compounds of the generic formula (I): $A[(XBX')_nB'Y]_p$, where Y comprises an arsenoxide group, and "A comprises at least one substantially cell-membrane impermeable pendant group selected from natural, unnatural, and synthetic amino acids, hydrophilic amines, peptides, polypeptides, thiol containing proteins, and oligosaccharides, or a combination thereof." The claims are also drawn to pharmaceutical compositions thereof.

(1) Level of skill and knowledge in the art:

The level of skill in the peptide arts is high, with regards to synthesis. With regards to the knowledge of biological effects, the art is unpredictable.

With regards to the effect of amino acid substitution in a peptide or protein, the art is unpredictable.

RUDINGER (J. Rudinger. In: Peptide Hormones, JA Parsons, Ed. (1976) 1-7) teaches that, "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study." (Page 6).

The effects of a single amino acid substitution can have substantial effects on proteins in structure and/or function and are exemplified by the difference between hemoglobin (Hb) and abnormal hemoglobins, such as sickle-cell hemoglobin (HbS). VOET (D. Voet and J.G. Voet. Biochemistry, 2nd Edition.(1995), pages 235-241) teaches that the mutant hemoglobin HbE [Glu B8(26)β → Lys] has, "no clinical manifestations in either heterozygotes or homozygotes." (Page 235). Further, Hb Boston and Hb Milwaukee both have single point mutations which result in altered binding affinity and ineffective transfer from the Fe(III) to Fe(II) oxidation state. Conversely, a single point mutation in Hb Yakima results in increased oxygen binding by the heme core, and in Hb Kansas, the mutation causes the heme center to remain in the T state upon binding oxygen (rather than structurally rearranging to the R state). (Page 236).

HbS is a single point mutation, Val → Glu A3(6)β (Page 236), which results in deformation and rigidity of the red blood cell. The mutation also provides protection against most malarial strains.

Further, SMILEK (D.E. Smilek, *et al.* Proc. Natl. Acad. Sci. USA (1991) 88, pages 9633-9637) teaches that a single amino acid substitution in the myelin basic protein peptide, "confers

the capacity to prevent rather than induce EAE even after peptide-specific encephalitogenic T-cells have been activated." (Abstract).

(2) Partial structure:

The specification and claims provide description of the structure of Y being As=O, and the structure of A being glutathione, glucosamine, cysteinylglycine, cysteic acid, aspartic acid, glutamic acid, lysine, or arginine.

The specification does not provide description for any species of Y comprising at least one arsenoxide, nor does the specification provide sufficient description to describe the myriad of compounds embraced by the generic moiety A. The specification and art do not provide sufficient description of the myriad of compounds embraced by the generic formula (I).

(3) Physical and/or chemical properties and (4) Functional characteristics:

The moiety, A, must be 'at least substantially cell-membrane impermeable'.

(5) Method of making the claimed invention:

The specification provides for making GSAO, and related compounds, but does not sufficiently describe how to make the myriad of compounds embraced by the generic claims.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claims 1, 11, 12, 14, and 38 are broad generics, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of cell-membrane impermeable pendant group linked to an arsenoxide comprising moiety. The specification lacks sufficient variety of species to reflect this variance in the genus, and while having written description of GSAO and compounds identified in the specification, figures, and/or examples,

the specification is void of sufficient variety of compounds to describe fully the genus embraced by formula (I).

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11, 12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by FAIRLAMB (PTO-1449, #2, 3/19/02) or MAES (US Patent 5,281,588).

The instant claims are drawn to the arsenoxide compounds, for the species shown above.

Fairlamb teaches the compound melarsen oxide (*materials and methods*, and footnote, page 2607)

Maes teaches the compound melarsen oxide structure (column 7, line 60).

Claims 1, 11, 12, 14, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by FLOC'H (US Patent 5,459,263).

The claims are presented *supra*.

Floc'H teaches the compound melarsen oxide in water (column 2, line 67- column 3, line 1) "the dry or wet melarsen oxide dihydrate is the suspended in water". Water is a pharmaceutically acceptable carrier, and in solution the dihydrate is no longer present, as would be the case in the solid form.

Allowable Subject Matter

Claims 9, 10, and 18-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: the closest prior art, Fairlamb, Maes, Floc'H, and/or WHITE (US Patent 2,951,766), each teach arsenoxide compounds but do not teach or suggest, alone or in combination, the compounds as instantly claimed in claims 9, 10, and 18-25.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

7/18/07
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PRIMARY EXAMINER

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Art Unit 1654